## REMARKS

In view of the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 43, 46, 47, 51 and 54 to 58, the only claims pending and currently under examination in this application.

## Rejections

### 35 U.S.C. § 112

Claims 43, 46, 47, 51 and 54-58 were rejected under 35 U.S.C. § 112, 1st ¶ for an asserted lack of sufficient written description. In making this rejection, the Examiner asserts that the specification is fails to provide sufficient written description for the full class of protease inhibitors as claimed.

In response, the Applicants respectfully point out that the term "serine protease inhibitor" is known in the art to refer to a class of compounds that all inhibit serine proteases. One of skill in the art can readily determine whether a given compound is a serine protease inhibitor by simply assaying that compound to determine whether it has serine protease inhibitory activity.

In addition, a number of different representative serine protease inhibitors are disclosed in the specification, as acknowledged by the Examiner.

Furthermore, the Applicants provide **in vivo** data showing the activity of AEBSF in rats in the "Kindling Assay." See Examples III and IV, pages 17 and 18, of the specification. AEBSF is representative of a broad class of agents that are collectively known as Serine Protease Inhibitors. See page 6, line 27 to page 7, line 4 of the specification. The Kindling Assay is an art accepted model of Epilepsy. These results demonstrate that AEBSF is effective in treating/preventing epilepsy.

In addition, based on studies in which the activity of AEBSF and other serine protease inhibitors are evaluated, one of skill in the art knows that the activity of AEBSF in a given assay is strongly indicative of the activity of other serine protease inhibitors in the assay. See e.g.: (1) Rideout et al., " Inhibitors of trypsin-like serine proteases prevent DNA damage-induced neuronal death by acting upstream of the mitochondrial checkpoint and of p53 induction," Neuroscience. 2001;107(2):339-52, where AEBSF and TLCK were shown to have analogous activity in the reported assay; (2) Singh et al., " Serine protease inhibitor causes F-actin redistribution and inhibition of calcium-mediated secretion in pancreatic acini," Gastroenterology. 2001 Jun;120(7):1818-27, where AEBSF and N(alpha)-p-tosyl-L-phenylalanine chloromethyl ketone (TPCK) were shown to have analogous activity in the reported assay; (3) Bestilny & Riabowol, "A role for serine proteases in mediating phorbol ester-induced differentiation of HL-60 cells," Exp Cell Res. 2000 Apr 10;256(1):264-71, where AEBSF, TLCK and TPCK were shown to have analogous activity in the reported assay; and (4) Stefanis et al., " Inhibitors of trypsin-like serine proteases inhibit processing of the caspase Nedd-2 and protect PC12 cells and sympathetic neurons from death evoked by withdrawal of trophic support," J Neurochem. 1997 Oct;69(4):1425-37, where AEBSF and TLCK were shown to have analogous activity in the reported assay.

Based on the above, there is no reason to think that serine protease inhibitors would act differently from each other in treating epilepsy. Furthermore, the Examiner has provided no evidence of such.

Accordingly, in view of knowledge of those of skill in the art as to the definition of a serine protease inhibitor, the description of various representative serine protease inhibitors and the in vivo results with a representative serine protease inhibitor that are fully predictive of results that would be achieved with other serine protease inhibitors, coupled with the Examiner's lack of any evidence showing that a given serine protease inhibitor will act differently from another in treating epilepsy, one of skill in the art would

recognize that, at the time the application was filed, the Applicants were in possession of the full scope of the claimed invention.

Accordingly, the rejection of Claims 43, 46, 47, 51 and 54-58 under 35 U.S.C. § 112, 1st ¶ for an asserted lack of sufficient written description may be withdrawn.

Next, Claims 43, 46, 47, 51 and 54-58 were rejected under 35 U.S.C. § 112, 1st ¶ for an asserted lack of enablement. In making this rejection, the Examiner's position appears to be based on the incorrect assumption that the Applicants have provided no in vivo data. As reviewed below, this assumption is incorrect because the Applicants do provide in vivo data in the experimental section with the representative compound AEBSF.

Again, the claimed methods are directed to treating or preventing epilepsy by administering an effective amount of a serine protease inhibitor.

In support of the enablement of these claims, the Applicants provide data showing the activity of AEBSF in rats in the "Kindling Assay." See Examples III and IV, pages 17 and 18, of the specification. The Kindling Assay is an art accepted model of Epilepsy. These results demonstrate that AEBSF is effective in treating/preventing epilepsy. **The kindling assay in rats is an in vivo assay.**

Furthermore, the specification teaches that AEBSF is representative of a broad class of agents that are collectively known as Serine Protease Inhibitors. See page 6, line 27 to page 7, line 4 of the specification.

Based on studies in which the activity of AEBSF and other serine protease inhibitors are evaluated, one of skill in the art knows that the activity of AEBSF in a given assay is strongly indicative of the activity of other serine protease inhibitors in the assay. See e.g.: (1) Rideout et al., " Inhibitors of trypsin-like serine proteases prevent DNA damage-induced neuronal death by acting upstream of the mitochondrial

checkpoint and of p53 induction," Neuroscience. 2001;107(2):339-52, where AEBSF and TLCK were shown to have analogous activity in the reported assay; (2) Singh et al., " Serine protease inhibitor causes F-actin redistribution and inhibition of calcium-mediated secretion in pancreatic acini," Gastroenterology. 2001 Jun;120(7):1818-27, where AEBSF and N(alpha)-p-tosyl-L-phenylalanine chloromethyl ketone (TPCK) were shown to have analogous activity in the reported assay; (3) Bestilny & Riabowol, "A role for serine proteases in mediating phorbol ester-induced differentiation of HL-60 cells," Exp Cell Res. 2000 Apr 10;256(1):264-71, where AEBSF, TLCK and TPCK were shown to have analogous activity in the reported assay; and (4) Stefanis et al., " Inhibitors of trypsin-like serine proteases inhibit processing of the caspase Nedd-2 and protect PC12 cells and sympathetic neurons from death evoked by withdrawal of trophic support," J Neurochem. 1997 Oct;69(4):1425-37, where AEBSF and TLCK were shown to have analogous activity in the reported assay. As such, one of skill in the art would expect, with a reasonable expectation of success, serine protease inhibitors other than AEBSF to act as AEBSF in the Kindling assay.

Accordingly, the claimed methods are fully enabled by the specification. As such, the objection to the specification and corresponding rejection of Claims 43, 46, 47, 51 and 54-58 under 35 U.S.C. § 112, 1st ¶ may be withdrawn.

In addition, Claims 55 and 57 have been rejected under 35 U.S.C. § 112, 2nd ¶ for the asserted reason that the term "like" in the claims is a relative term rendering the claims indefinite. However, the claims recite "trypsin-like serine protease." As such, the term "like" is not used by itself, but instead in the phrase "trypsin-like" which then describes the type of serine protease.

The phrase "trypsin-like serine protease" has been used for a long time in the art to refer to a class of proteases, and pone of skill in the art readily knows what is meant by this phrase. Evidence of this well known phrase can be found by entering the phrase "trypsin-like serine protease" into the search field of PUBMED, which action results in 171 hits, dating as far back as 1980. An example of one of these hits is:

Kramer MD, Binninger L, Schirrmacher V, Moll H, Prester M, Nerz G, Simon MM. Characterization and isolation of a **trypsin-like serine protease** from a long-term culture cytolytic T cell line and its expression by functionally distinct T cells. J Immunol. 1986 Jun 15;136(12):4644-51.

As such, the term "like" in Claims 55 and 57 does not render these claims indefinite and the rejection of these claims under 35 U.S.C. § 112, 2nd ¶ may be withdrawn.

**35 U.S.C. § 102**

Claims 43, 46, 47, 51 and 54-58 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Strickland, U.S. Patent No. 5,786,187. However, **no inhibitors** of serine proteases or tPA were actually tested in this patent. Instead, the Strickland reference is merely a description of a knockout animal and then "guesses" are made based on the phenotype of the animal.

As such, Strickland does not actually **administer an amount of a serine protease inhibitor to any host or subject, much less to a subject to treat the animal for epilepsy, as is currently claimed.**

Because Strickland does not actually administer an amount of a serine protease inhibitor to a subject, Strickland does not anticipate the claimed methods.

In addition, Strickland cannot be viewed as enabling the claimed methods. Without actual data from an art recognized model, such as the kindling assay employed in the Experimental Section of the present application, there can be no enablement of a method of treating epilepsy by administering a serine protease inhibitor.

Accordingly, because Strickland doe not actually administer a serine protease inhibitor to treat a host for epilepsy or enable such a method, the claimed methods are not anticipated by Strickland and this rejection may be withdrawn.

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## CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number THUR-001.

Respectfully submitted,
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Date: September 12, 2005

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